IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 6 Ver. 4 (June. 2018), PP 14-18
www.iosrjournals.org

Thyroid Profile in Patients with Metabolic Syndrome

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Abstract:
Background: *Metabolic syndrome (MS) is a cluster of metabolic abnormalities. MS and hypothyroidism are associated with increased risk of atherosclerotic heart disease. Insulin resistance is the central pathophysiological phenomenon underlying the clustering.*
Aims and Objective: *To study the association, prevalence and types of thyroid dysfunction in patients with MS*
Materials and Methods: *A Non-randomized Cross sectional study was done at Institute of Internal Medicine, Madras medical college and Rajiv Gandhi government general hospital, Chennai from January 2018 to April 2018. A total 0f 60 patients with MS selected according to WHO criteria were studied .Patients were evaluated based on anthropometry, evaluation of vital parameters, fasting blood sugar, lipid and thyroid profile. Statistical analysis were done using SPSS software 22.0*
Results: *Among 60 patients there were 45% males and 55% females. The thyroid dysfunction is 16.7% prevalent in MS, of which Subclinical hypothyroidism (SCH) was more prevalent (11.7%) compared to overt hypothyroidism (3.3%) and subclinical hyperthyroidism (1.7%).*
Conclusion: *There was a significant prevalence of thyroid dysfunction in MS. Hence Thyroid function test (TFT) must be done in all patients with MS to assess thyroid function.*
Keywords: *Metabolic syndrome Thyroid dysfunction, Subclinical hypothyroidism, Thyroid function test*

Date of Submission: 25-05-2018 Date Of Acceptance: 08-06-2018

I. Introduction

Metabolic syndrome (MS) is a cluster of metabolic abnormalities wherein people are obese and have hypertension, high triglyceride level, low high density lipoprotein (HDL) and abnormal fasting glucose levels [(1,2).] People with MS are at high risk for developing cardiovascular disease.[(3)] Insulin resistance is supposed to be the central pathophysiological phenomenon underlying the clustering.[(4)]

Thyroid disease is associated with atherosclerotic cardiovascular disease.[(5-8)] This association may be in part explained by thyroid hormone's regulation of lipid metabolism and its effect on blood pressure. Thyroid hormones have ubiquitous effects and influence the function of most organs. This hormone appears to serve as a general pacemaker accelerating metabolic process and may be associated with MS.[(9)]

Both MS and thyroid dysfunction are associated with increased risk of atherosclerotic heart disease.Only few studies have been performed .[(10.11)] In a cross sectional study in 220 MS patients, it was found that subclinical hypothyroidism was prevalent in 16.4% of MS patients.[(10)] In one study , it was found that metabolic syndrome was prevalent in thyroid dysfunction patients .[(11)] This study was carried out to find the association of thyroid dysfunction in MS patients.

II. Aims And Objectives

To study the association, prevalence and types of thyroid dysfunction in patients with MS

III. Methodology

Study design :
Non randomized Cross sectional study
Study centre :
Institute of Internal medicine, Madras medical college and Rajiv Gandhi Government General Hospital, Chennai
Study duration :
January 2018 to April 2018 – 4 months
Sample size :
60 patients after applying inclusion and exclusion criteria

Selection of study Subjects

Patients with MS were selected as defined by WHO, require the presence of any one of the criteria from diabetes mellitus (DM), impaired glucose tolerance, impaired fasting glucose or insulin resistance and any two of the risk factors [blood pressure (BP) ≥130 /85 mmHg, dyslipidemia (TG ≥150 mg/dl, HDL-C <40 mg/dl in male and <50 mg/dl in female, waist to hip ratio > 0.85 in male, >0.90 in female and BMI >30 kg/m_2 and urinary albumin excretion > 20 μg/min or albumin to creatinine ratio > 30 mg/g).

Inclusion criteria :

MS patients not on any medications and newly detected MS patients

Exclusion criteria :

1. Known Hypothyroid/ SCH
2. Taking Medications for DM/SHT/Thyroid Disorder
3.Taking Steroids
4. Severely ill patients
5. Pregnant Women
6. Individuals below 18 yrs

A detailed history of patients medications and anthropometric measurements like height, waist circumference were noted in a semi-structured proforma. Blood pressure was recorded in right upper limb in sitting posture. Blood samples were obtained after a 12 hour overnight fast for biochemical analysis [fasting blood sugar, lipid profile, free T4 and thyroid stimulating hormone (TSH)]. The fasting blood sugar was done by enzymatic calorimetric method using semi auto analyser.The Lipid profile were done enzymatically on XL-300 ERBAfully automated clinical chemistry analyser. The thyroid hormone assay were done by Chemiluminescence Immuno assay (CLIA) using ADVIA Centauraequipment.

In this study Euthyroidism is defined as TSH concentration of 0.4 mU/L to 4.5mU/L and fT4 concentration of 0.7 ng/dl to 1.8 ng/dl. SCH was defined as a TSH concentration of 4.51 mU/L to 10 mU/L with a normal fT4 concentration (0.7 ng/dl to 1.8 ng/dl). Hypothyroidism was defined as a TSH concentration of more than 10mU/mL with an fT4 concentration level below normal (<0.7 ng/dl). Subclinical hyperthyroidism is defined as TSH concentration of 0.1 mU/L to 0.4 mU/L and fT4 concentration of 0.7 ng/dl to 1.8 ng/dl. Hyperthyroidism is defined as a TSH concentration of less than 0.1mU/L with an elevated fT4 of >1.8 ng/dl. Data was compiled and analysed using IBM SPSS ver. 22.0. Categorical data was compared using percentages and student 't' test was used wherever required. P values less than 0.05 was considered significant.

Limitations of the study:

1) Small number of study subjects.
2) fT3 levels not assessed

IV. Results

Among the 60 patients included in our study, 27 were men (45%) and 33 were women (55%) of the total cases According to the age, patient's between 30 and 39 years of age were 15(25%). Majority were in the age group 40-49 years – 28 patients (47%). 11 patients (18%) were in the age of 50-59 years and 6 patients (10%) were above the age of 60 years .[Table 1] According to the MS parameters , out of 60 patients 19 fulfilled 3 among 5 MS parameters criteria, another 19 members fulfilled 4 MS parameters criteria and the rest 22 members fulfilled all the MS criteria.

The TSH in this study was ranging from 0.17mU/L to 150 mU/L and free T4 levels ranging from 0.16ng/dl to 1.68ng/dl. Patients were grouped into 4 groups according to the definitions based on TSH and fT4 levels and further statistical analysis was done based on these groups. According to our definitions, 50 patients found to be euthyroid and 2 patients were hypothyroid. 7 patients had SCH and 1 patient had Subclinical hyperthyroidism, there were no overt hyperthyroid patients in our study.

The thyroid dysfunction is 16.7% prevalent in MS patients. Among the thyroid dysfunction , SCH is highly prevalent (11.7%). The hypothyroidism is 3.3% prevalent in MS patients (1 patient had TSH levels of >150mU/L) and SCH is 1.7% prevalent. There were no overt hyperthyroidism patients in our study.[Table 2] According to the age, patients age between 30 and 39 years were 15 in number, among them one had frank hypothyroidism and 1 patient had subclinical hypothyroidism. In the 40-49 years age group, 4 patients had SCH and 1 had subclinical hyperthyroidism. In the 50-59 years of age group, 1 patient had frank hypothyroidism and 2 patients had SCH. In the above age of 60 years , all 6 patients were normal..[Table 3].

Based on the metabolic syndrome criteria, of those patients who fulfilled 3 out of 5 risk factors 3 had thyroid dysfunction, of the patients who had 4 risk factors 2 had thyroid dysfunction, of the patients who had all 5 risk factors 5 had thyroid dysfunction.[Table 4]

As there were a considerable number of patients only in both Euthyroid group (50) and SCH group (7), both groups were analysed using student t- test. But these analyses were not statistically significant, as there were very small number of individuals in both subgroups and variants are very high in both subgroups. Table 5 Correlation between fT4, TSH and metabolic parameters in both subgroups were also also analysed. Table 6-7 As there were limited number of subjects with very high variants , statistically significant results were not found.

Table 1 Population Characteristics

AGE (Years)	TOTAL NO.	PERCENTAGE	MALE	FEMALE
30 - 39	15	25%	6	9
40 - 49	28	47%	14	14
50 - 59	11	18%	1	10
60 - 69	6	10%	6	0

Table 2 Thyroid Dysfunction

GROUP	TOTAL NO.	PERCENTAGE	MALE	FEMALE
EUTHYROID	50	83.33%	26	24
HYPOTHYROID	2	3.33%	1	1
SCH	7	11.67%	0	7
SUBCLINICAL HYPERTHYROIDISM	1	1.67%	0	1
HYPERTHYROIDISM	0	0	0	0

Table 3 Age wise Thyroid Dysfunction

AGE (Years)	TOTAL NO.	EUTHYROID	HYPOTHYROID	SCH	SUBCLINICAL HYPERTHYROID
30-39	15	13	1	1	0
40-49	28	23	0	4	1
50-59	11	8	1	2	0
60-69	6	6	0	0	0

Table 4 MS Parameters wise Thyroid Dysfunction

MS CRITERIA FULFILLED	TOTAL NO.	EUTHYROID	HYPOTHYROID	SCH	SUBCLINICAL HYPERTHYROID
3	19	16	1	2	0
4	19	17	0	1	1
5	22	17	1	4	0

Table 5 Distribution of Thyroid Dysfunction

MS PARAMETERS	EUTHYROID		SCH		P VALUE
	MEAN	SD	MEAN	SD	
WC	97.16	6.98	98.57	8.32	0.626
SBP	139.88	14.14	140.29	14.40	0.944
DBP	89.52	7.28	88.29	9.20	0.689
FBS	158.28	51.04	141.43	37.82	0.405
HDL	43.46	6.25	43.43	4.58	0.990
TGL	234.20	170.18	185.57	93.75	0.434

(P Value >0.05 Not significant at 5% level)

WC – Waist Circumference, SBP – Systolic Blood Pressure, DBP – Diastolic Blood Pressure, FBS – Fasting Blood Sugar, HDL – High Density Lipoprotein, TGL – Triglycerides

Table 6 Correlation between fT4, TSH and MS parameters in Euthyroid patients

MS PARAMETER	fT4	P Value	TSH	P Value
WC	0.243	0.08	- 0.029	0.839
SBP	0.078	0.59	0.076	0.60
DBP	0.125	0.38	- 0.416	0.77
FBS	0.175	0.22	- 0.095	0.59
HDL	0.067	0.64	- 0.108	0.45
TGL	0.056	0.69	- 0.066	0.30

(P Value > 0.05 Not significant at 5% level)

Table 7 Correlation between fT4, TSH and MS parameters in SCH patients

MS PARAMETER	fT4	P Value	TSH	P Value
WC	0.650	0.11	- 0.577	0.17
SBP	0.514	0.23	- 0.511	0.24
DBP	- 0.049	0.91	0.060	0.89
FBS	0.741	0.05	- 0.576	0.17
HDL	0.460	0.29	- 0.249	0.58
TGL	- 0.104	0.82	- 0.134	0.77

(P Value > 0.05 Not significant at 5% level)

V. V. Discussion

The metabolic syndrome is a cluster of metabolic abnormalities wherein people are obese and have hypertension, high TGL level, low HDL and abnormal fasting glucose levels.[4] People with MS are at high risk for developing cardiovascular disease and type 2 Diabetes. Hypothyroidism is associated with lipid abnormalities like high TGL and low HDL, weight gain, glucose intolerance and hypertension.[12] Thus hypothyroidism mimics the parameters of MS.

In this study, thyroid dysfunction prevalence is 16.7% among MS patients. Hypothyroidism is 15% prevalent in metabolic syndrome patients (Overt Hypothyroidism 3.3% and SCH 11.7 %). The prevalence of thyroid dysfunction and hypothyroidism in metabolic syndrome patients are higher than the prevalence in normal population, which is 5.9% for thyroid dysfunction and 4.6% for hypothyroidism (0.3% overt and 4.3% SCH).[13] This study is consistent with study done by Uzunulu et al, as 16.4% of MS patients had hypothyroidism in Japan.[10] In this study prevalence of subclinical hyperthyroidism is 1.7% and there is no overt or clinical hyperthyroidism.

In this study $1/6^{th}$ of MS patients or every 6^{th} patient with MS has hypothyroidism . In these hypothyroidism patients, treatment with levothyroxine replacement reverses the symptoms and signs of hypothyroidism, thereby those factors which mimic MS.

It is well known and proven that, by treating with levothyroxine replacement in all overt or clinical hypothyroid patients, we can reduce all the metabolic parameters and cardiovascular risk.[12] There is some controversy in treating SCH patients.[35,44,46]

The risk of progression from SCH to overt hypothyroid is 2 – 5% per year.[14] A meta-analysis report shows that levothyroxine therapy in individuals with SCH lowers mean serum total and low density cholesterol concentration significantly and the reduction in serum cholesterol may be larger in individuals with higher pretreatment cholesterol levels. [15] Another double blind placebo-controlled trial (Basal Thyroid Study) shows that an important risk reduction of cardiovascular mortality of 9 – 31% possible by improvement in low density lipoprotein cholesterol in SCH patients treated with levothyroxine therapy. [16,17]

Surks et al., recommends treating SCH associated with T2DM and SHT in his scientific review.[14] As the MS patients have hyperlipidemia, diabetes, hypertension and increased cardiovascular risk, it looks logical to treat MS patients having SCH by levothyroxine replacement therapy.While there appears to be no adverse effects of initiating levothyroxine treatment in this setting, inadvertent overtreatment occurs in 14 - 21% of levothyroxine treated patients, [17,18] carrying potential risks of osteoporosis and atrial fibrillation when serum TSH falls below 0.1mU/L.[19] These patient need frequent thyroid function tests to avoid this complication.

This study shows that prevalence of thyroid dysfunction in MS patients is higher than in normal subjects. $1/6^{th}$ of MS patients or every 6^{th} MS had hypothyroidism either overt or subclinical. This finding indicates a need for investigating the presence of Thyroid dysfunction during managing MS patients. As shown in previous evidences, managing these hypothyroid in MS patients are rewarding by improvement in the metabolic parameters and reducing cardiovascular risk.

VI. Conclusions

Thyroid dysfunction occurs in MS patients. Thyroid dysfunction occurs in 16.7% of MS patients. Prevalence of hypothyroidism is 15.0% (overt hypothyroidism 3.3% and SCH 11.7%) in MS patients which is higher than that of general population. $1/6^{th}$ of MS or every 6^{th} MS had hypothyroidism either overt or subclinical. Hence we should do a thyroid function test to assess thyroid dysfunction while managing MS patients.

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Prof Dr.K.S.Chenthil MD "Thyroid Profile in Patients with Metabolic Syndrome."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 6, 2018, pp 14-18.